The Results of Hemoglobinopathy Screening in Hatay, the Southern Part of Turkey

Türkiye'nin Güneyinde Hatay'da Hemoglobinopati Tarama Sonuçları

Hemoglobinopathy Screeningin Hatay

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Özet

Amaç: β-Talasemi ve hemoglobinopatiler yaygın genetik bozukluklardır. Bu nedenle evlilik öncesi çiftler ya da her anemik kişi rutin hemoglobinopatiler açısından incelenmelidir. Bu retrospektif çalışmada amacımız, β-talasemi ve hemoglobinopati sıklığını Türkiye'nin güney kesiminde bulunan Hatay'da, saptamaktır. Gereç ve Yöntem: Bu çalışmada veriler, Ocak 2006 ve Ekim 2012 tarihleri arasında anemi nedeni ile ve evlilik öncesi araştırma için Hatay Antakya Devlet Hastanesi Hemoglobinopati Merkezi'ne başvuran 70226 bireyden alınmıştır. Kan örnekleri EDTA'lı tüplere alınmış ve hematolojik parametreler bir Sysmex XT-2000i Hematology Analyzer kullanılarak analiz edilmiştir. Yüksek performanslı sıvı kromatografisi tekniği hemoglobin tiplerini belirlemek için kullanılmıştır. Bulgular: Hemoglobinopati sıklığı β-Talasemi taşıyıcılığı % 6, orak hücre anemisi taşıyıcılığı %6,3, α-talasemi taşıyıcılığı? %12,9 ve diğer anormal hemoglobinopatili varyantları % 4,2 idi. Homozigot β-talasemi 49 olguda, homozigot hemoglobin S 60 olguda, HbH hastalığı (bir talasemi intermedia) 33 olguda tespit ettik. Tartışma: β-talasemi taşıyıcılığı ve diğer hemoglobinopati sıklığının Hatay'da Türkiye'de diğer iller ile karşılaştırıldığında oldukça yüksek olduğu bulunmuştur.

Anahtar Kelimeler

Hemoglobinopati Taraması; β-Talasemi; Orak Hücreli Anemisi

Abstract

Aim: β-Thalassemia and hemoglobinopathies are common genetic disorders in Turkey. Because of this reason, either anemic people or couples before marriage are investigated for hemoglobinopathies routinly. In this retrospective study, our aim was to determine the frequency of β-thalassemia and hemoglobinopathies in Hatay, which is located in the southern part of Turkey. Material and Method: In this study, data from 70226 individuals, admitted to Antakya State Hospital Hemoglobinopathy Center in Hatay, both for the reason of anemia and before marriage investigations, were evaluated between January 2006 and October 2012. The blood samples were collected into EDTA-containing tubes and hematological parameters were analyzed using a Sysmex XT-2000i Hematology Analyzer. High performance liquid chromatography technique was used to determine the type of hemoglobin. Results: The frequency of hemoglobinopaties were 6% β-Thalassemia trait, 6.3% sickle cell trait, 12.9% α-thalassaemia trait? and 4.2 % other abnormal hemoglobinopaties variants. We detected 49 cases with homozygot β-thalassaemia, 60 cases with homozygot haemoglobin S, 33 cases with HbH disease (thalassaemia intermedia) among all. Discussion: The frequency of β-thalassemia trait and other haemoglobinopathies in Hatay is found to be quite high as compared with other provinces in Turkey.

Keywords

Hemoglobinopathy Screening; B-Thalassemia; Sickle Cell Anemia.

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Introduction

Sickle cell disease (SCD) and thalassemia are the most common inherited causes of anemia. Sickle cell disease is caused by a single amino acid mutation with substitution of valine for glutamic acid at position 6 on the β- globin chain. The most common symptom of SCD is acute pain, but it is a multi-organ disorder and long-term follow up is required. The group includes homozygous SCD (HbSS), and compound heterozygotes for hemoglobin S and hemoglobin C (HbSC disease), hemoglobin S and β-thalassemia, (HbSβ- thalassemia), and other rare hemoglobin variants [1,2].

β-Thalassemia is an autosomal recessive disorder characterized by microcytosis and hemolytic anemia, which is a result of the reduced synthesis of the β–globin chains of hemoglobin. β-thalassemia major is the most clinically significant of the thalassemias and requires lifelong transfusion therapy, that will result in iron overload and subsequent clinical problems unless iron chelation therapy is undertaken [1,2]. The disorder affects about 150 million people in Mediterranean, West Africa, and large parts of Asia. Turkey is one of the largest countries of the Middle East occupying the whole of classical Asia Minor (Anatolia) and a small portion of Eastern Thrace in Europe [2]. Similarly, hemoglobinopathies are common in different ethnic groups and in a broad geographic area including Equatorial Africa, Southern Turkey, Saudi Arabia, Southern India, and Greece. Mersin and Antakya, two other cities located in the Cukurova Region, also have a high rate of β-Thalassemia and hemoglobinopathies [3]. β-Thalassemia is a heterogeneous disorder which is often classified into classical (characterised by elevated levels of HbA2 and HbF) and silent (normal HbA2 ± elevated HbF) types. Subjects were considered to have β-Thalassemia trait if mean corpuscular volume was <79 fl, mean corpuscular haemoglobin<27 pg and haemoglobin A2 level >3.5%. In order to find out the silent types, patients who have normal HbA2 values and HbF values>2% required molecular analysis [4,5].

α-thalassemia is caused by the loss of one or more of the four α chains. A one or two gene deletion leads to α-thalassemia trait, a three-gene deletion to HbH disease (thalassemia intermedia) and a four-gene deletion to hydrops fetalis, which is usually fatal in utero [1]. Alpha thalassaemia is most frequently suspected initially on the basis of a routine full blood count. All affected individuals have a variable degree of anaemia (Hb), reduced mean corpuscular haemoglobin (MCH/pg), reduced mean corpuscular volume (MCV/fl) and a normal or slightly reduced level of the minor HbA2. Molecular analysis is usually required to confirm the haematological observations (especially in silent alpha-thalassaemia and alpha-thalassaemia trait) [6].

Thalasemias and SCD are common diseases in Turkey. This study aimed to find out the spectrum and distribution of hemoglobinopatnies in Hatay, a place in Cukurova Region where there is a high rate of β-Thalassemia, SCD and hemoglobinopathies.

Material and Method

In this retrospective study, data from 70226 individuals, who were admitted to Antakya State Hospital Hemoglobinopathy Center in Hatay and other different cilinics in the center of the city, both for the reason of anemia and before marriage investigations for screening of thalassemia carriage, were evaluated between January 2006 and October 2012.

Clinical data were obtained from patients' medical charts. Blood samples were collected in EDTA containing tubes for estimation of hemoglobin (Hb), mean cell volume (MCV) and mean cell hemoglobin (MCH). The tests were performed on a Sysmex XT-2000i Hematology Analyzer (USA). We analyzed all samples on the Bio-Rad Variant II high performance liquid chromatography (HPLC) system with a Variant II β-Thalassemia Short Program Reorder Pack (Bio-Rad Laboratories) in same day. The subjects were considered to have the β-thalassemia trait if they had a mean corpuscular volume (MCV) <80 fL and/ or a mean corpuscular hemoglobin (MCH) level of <27 pg and a hemoglobin (Hb) A2 level of >3.5% (7). Molecular analysis were recommended on patients who thought to be Silent types β-Thalassemia. This group was not included in the β-thalassemia trait group. Concurrently patients who were considered as alpha-thalassaemia trait? also had the same molecular analysis. HbF, S, C, D, E and other variants were also detected.

All data analyses were performed using SPSS software, version 15.

Results

Overall, of total 70226 people, 52% were female and 48% were male. A percentage of 73 of all were premarital screening. The frequencies of β-thalassemia trait, sickle cell trait, α-thalassemia trait?, HbC trait, HbD trait and HbE trait were 6%, 6.3%, 12.9%, 0.15%, 0.16% and 0.21% respectively. Other rare variants were found 0.04% (n=27) (Hb O-Arap, Hb G-Copenhagen, Hb J-Baltimore, Hb Manitoba, Hb Hasheron, Hb Athens-Georgio and Hb J-Norfolk).

We determined 161 cases with homozygosit hemoglobinopaties among 70226 individuals. Among the 161 cases with homozygosit hemoglobinopaties, 60 cases were diagnosed as sickle cell homozygotes (37.2%), 49 cases were β- thalassemia major (30.5%), 33 cases were HbH disease (20.5%), 3 cases were HbCC disease (1.9%), 3 cases were HbDD disease (1.9%), 3 cases were HbEE disease (1.9%) and 10 cases were HbS/HbE (6.1%) (Table I). The distribution of patients newly diagnosed as homozygote hemoglobinopathies are shown according to date of birth in Figure 1.

Table I. Distribution according to years of patients with homozygotic hemoglobinopaties newly diagnosed

Year	Sickle cell disease n (%)	Thalassemia major n (%)	Hb H disease n (%)	Hb CC n (%)	Hb DD n (%)	Hb EE n (%)	Hb SE n (%)	n
2006	11(0.08%)	11(0.08%)	8 (0.06%)	1(0.01%)			6(0.04%)	13345
2007	15(0.11%)	6 (0.05%)	6(0.05%)	1(0.01%)	2(0.02%)	1(0.01%)	3(0.02%)	13097
2008	6 (0.07%)	7(0.08%)	2 (0.02%)		1(0.01%)	1(0.01%)	1(0.01%)	8801
2009	10 (0.13%)	5(0.07%)	5(0.07%)					7508
2010	5 (0.06%)	6(0.07%)	5(0.05%)					8160
2011	5 (0.05%)	7(0.07%)	4 (0.04%)	1(0.01%)				9956
2012	8 (0.09%)	7(0.07%)	3 (0.03%)			1(0.01%)		9359
Total	60(0.09%)	49(0.07%)	33(0.05%)	3(0.004%)	3(0.004%)	3(0.004%)	10(0.01%)	70226

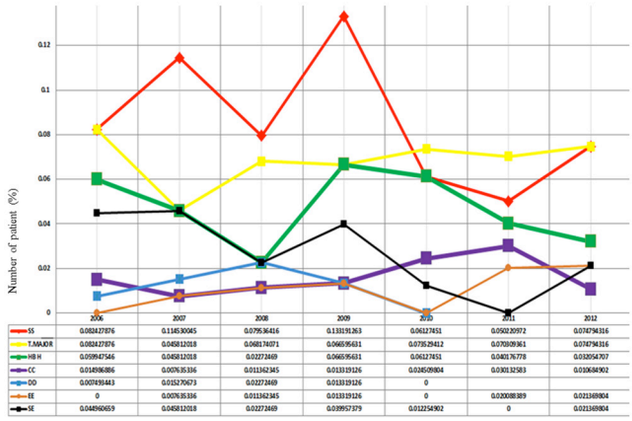

Figure 1. Distribution according to date of birth of patients with homozygosity hemoglobinopathies newly diagnosed.

Discussion

Hemoglobinopathies are the most important health problems in Hatay. In countries with a high prevalence of haemoglobinopathies, premarital screening programmes are helpful to identify haemoglobinopathies and to inform marital partners [8]. In our country the premarital screening programs, especially in the regions with high risk, reduced the number of risky newborns with thalassemia and SCD [9,10].

About 150 million people worldwide carry beta-thalassemia gene. The beta thalassemia trait genes frequency are Sardinia (11 to 34%) [11], and Iran (4 to 10%) [12]. The prevalence of beta-thalassemia trait and sickle cell anemia trait in premarital screening program in Saudi Arabia were 1.8% and 4.5% [13].

The average frequency of the β-thalassemia trait has been reported as approximately 4.3% in Turkey. The highest prevalence of the beta-thalassemia trait (13.1%) was found in the Antalya region and of the HbS trait (10%) in the Cukurova region [10]. The ratio of β-thalassemia trait is 3.1% around Icel, 2.6% in Denizli, 2% in Konya, 0.68%, in Erzurum, 2.3% in Kahramanmaras and 0.89% in Kocaeli while SCD trait ratio is reported as; 6.4%, around Icel, 0.11% in Denizli, 0.05% in Konya, 0% in Erzurum, 0.54% in Kahramanmaras and 0.05% in Kocaeli [7, 14-18].

The previous studies in our region showed the high ratios of SCD and β-thalassemia [19-21]. The incidence of sickle cell trait is 10.0% and β-thalassemia trait is 3.7% in the Cukurova region in the southern Turkey. Sickle cell anemia is prevalent in the Cukurova region, but β-thalassemia is seen all over the country [22,23]. A research on 10207 individuals screened in Hatay, showed that 8% had sickle cell trait, 3% had β-thalassemia trait [9]. In our study we determined 6% β-thalassemia trait, 6.3% sickle cell trait. The β-thalassemia trait ratios are equivalent to the ratios from other parts of Turkey and Health ministry reports. Our study revealed out that SCD trait ratio decreased while β-thalassemia trait increased as compared with another study done in our center [9]. Currently the majority of the population in Hatay is of Arab origin, known as “Eti-Turks”, whose ancestors immigrated from Syria centuries ago. Therefore, the prevalence of HbS has been found to be considerably high in these areas compared to other parts of Turkey. In addition, consanguineous marriages are seen in a high incidence in these provinces, which also contributes to the increased frequency of HbS and HbE heterozygotes [21,24]. Sarper et al [7] showed that 0.09% had HbD trait, 0.09% had HbC trait. Acemoglu et al [17] detected that hemoglobin D was the most common (0.12%) abnormal hemoglobin. Hemoglobins S, C and E were not detected [17]. Moreover, HbD Punjab and HbO Arab has been reported to be the most common Hb variants after β-thalassemia trait with frequencies of 0.36% and 0.09%, respectively in Kayseri [25]. In our study HbD trait, HbC trait and HbE trait were at the ratio of 0.16%, 0.15% and 0.21% respectively. Other rare variants were found as 0.04% (Hb O-Arap, Hb G-Copenhagen, Hb J-Baltimore, Hb Manitoba, Hb Hasheron, Hb Athens-Georgio and Hb J-Norfolk). In our study other rare variants ratios were higher than in the study of Sarper and Acemoğlu while it was lower than in Karakukcu et al.

According to our results in some of our regions (9.8% Hassa, 6.4% Antakya centrum and 6.1% Altinozu,) β-thalassemia trait ratios are higher, while in some of them (%11.3 Samandag, %5.7 Antakya centrum and %6.6 Iskenderun) SCD trait ratios were higher than the average of Turkey. This is mainly because of the ethnic origin and population differs from district in Hatay. Besides consanguineous marriages are seen in a high incidence in these provinces and so that the carrier and trait ratios will increase.

Conclusion

The incidence of SCD and β-thalassemia major is increasing in the Hatay because of greater migration, and consanguineous marriages. Our results indicate that hemoglobinopathies still appear to be an important public health problem in Hatay. Because consanguineous marriages are very common in this area, genetic counseling should be provided for premarital couples to prevent homozygote births. That is why the screening programs are so important for our region. Abnormal hemoglobin screening programs must include education, counseling aspects and treatment facilities. Screening can be done by governmental, private, or other public programs, but must be on a voluntary basis. We aimed to keep the goverment and peoples informed in the light of our results.

Competing interests

The authors declare that they have no competing interests.

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